

Please add claims 39 and 40.

-- 39. The isolated nucleic acid molecule of claim 1, wherein the molecule hybridizes in 6× SSC at about 45°C, followed by one or more washes in 0.2× SSC, 0.1% SDS at 50°C with a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 45 or 46 or a complement thereof.

40. The method of claim 12, wherein the polypeptide exhibits lipase activity. --

## Remarks

Claims 1-7, 12, and 24-40 are pending. Claims 1, 12, 30, 32, and 37 have been amended. Claims 39 and 40 have been added. The amendments and additions made to the claims do not include new matter, as set forth in the ensuing section of this Amendment.

### Support in the Specification

The stringent conditions added to claims 1, 12, 32, and 37 and included in newly added claim 39 are disclosed in the specification, for example at page 76, lines 8-11.

Recitation in claims 1, 12, and 30 of at least 20 consecutive amino acid residues is supported in the specification, for example at page 3, lines 11-18.

The recitation in newly added claim 40 that the polypeptide exhibits lipase activity is supported in the specification, for example at page 64, lines 29 and 30.

### References Cited on Form PTO-1449

The Examiner indicated that copies of the references cited on the form PTO-1449 filed with Paper No. 4 did not accompany the form, but would be considered if new copies were forwarded to the Examiner's attention. A new copy of the form PTO-1449 filed with Paper No. 4, a copy of the form PTO-1449 filed with the Supplemental Information Disclosure Statement sent by the Applicants on November 2, 2000, and copies of the references cited on the two PTO-1449 forms are being submitted to the Examiner under separate cover (owing to their bulk). Consideration and acknowledgment of the references cited on the forms PTO-1449 are

respectfully requested. The Examiner is requested to forward initialed copies of the forms PTO-1449 with the next communication for this application.

### **New Declaration**

A newly executed Declaration and Power of Attorney, signed in full by the inventors, accompanies this Amendment. The Applicants believe that submission of this executed document overcomes the Examiner's objection to the Declaration.

### **Objections and Rejections Pursuant to 35 U.S.C. §101**

The Examiner rejects all of the pending claims pursuant to 35 U.S.C. § 101. The Examiner appears to accept that the uses asserted for the claimed nucleic acid molecules are substantial and specific (Office Action, page 4, first full sentence). However, in the Examiner's view, the Applicants have failed to establish a credible utility for the nucleic acid molecules recited in the claims. The Examiner appears willing to accept that if the Applicants establish a credible utility for TANGO 294 protein, then that would establish that the claimed nucleic acids also have a credible (and substantial and specific) utility.

The Examiner recognizes that the Applicants have disclosed nucleotide sequences (SEQ ID NOS: 45 and 46) that encode a protein designated TANGO 294 that is expressed in humans and that has the amino acid sequence SEQ ID NO: 47. The Examiner also recognizes that the Applicants assert that TANGO 294 has various activities, including involvement in absorption and metabolism of fat and various fat- and lipid metabolism-related disorders. However, the Examiner does not believe that the assertion that TANGO 294 has these activities can credibly be made, based solely on amino acid sequence similarity between TANGO 294 and known lipases.

The Applicants point out that it is well known in the art that absorption and metabolism of fats and lipids by humans can have seriously adverse health consequences, even in the absence of an existing disease or disorder in the human. Furthermore, it is well known that lipases are one of the classes of enzymes involved in uptake, interconversion, and metabolism of lipids. It is also well established that modulation of lipase expression and activity can modulate lipid uptake and metabolism in humans, and that modulation of lipid uptake and metabolism in

humans can mitigate, reduce, or prevent the adverse health consequences associated with lipid absorption and metabolism. A skilled artisan would accept that nucleic acids encoding a lipase (as well as the complements of those nucleic acids) could be used to modulate expression and activity of the lipase and to make and screen other compounds useful for modulating expression and activity of the lipase. For these reasons, the Applicants assert (and the Examiner appears to recognize) that if they establish that TANGO 294 protein is a lipase, then that is sufficient to demonstrate that the claimed nucleic acid molecules have a specific, substantial, and credible utility.

The Applicants respectfully believe that the Examiner has overlooked the most direct assertion of utility for TANGO 294 protein and nucleic acids encoding all or a portion of it. At page 64, lines 29 and 30 of the specification, the Applicants disclose that TANGO 294 protein is a lipase (i.e., an enzyme that exhibits lipase activity). The Examiner appears to believe that the Applicants' assertions regarding TANGO 294 utility is based solely on overall amino acid similarity between TANGO 294 and known lipases, as evidenced by the Examiner's comments regarding the occasional disparity in the field between sequence homology and functional similarity. However, the Applicants' assertion that TANGO 294 exhibits lipase activity is not based solely on overall sequence homology.

In addition to the significant overall amino acid sequence homology that TANGO 294 shares with other mammalian lipases, the amino acid sequence of TANGO 294 protein includes specific functional amino acid sequences and residues conserved among lipases, including the lipase serine active site (residues 180-189), the amino acid residues that form the catalytic triad of the lipase active site (residues 186, 357, and 386), two cysteine residues conserved among lipases (residues 260 and 269), and two conserved residues that form an oxyanion hole in lipases (residues 100 and 187). Furthermore, the Applicants have enclosed with this Amendment a phylogenetic tree that shows the relationship of TANGO 294 amino acid sequence (identified as "Fbh46692 126 1397" and indicated with an arrow) with the top BLAST hits in a public protein sequence database. All of the proteins shown in the phylogenetic tree for which activities have been established (indicated by stars) are lipases, sterol hydrolases (which catalyze deacylation of a sterol - a reaction analogous to lipase activity, which is deacylation of a lipid), or both. In view of all of these similarities between TANGO 294 and known lipases, the

skilled artisan would accept that TANGO 294 is a lipase. The Applicants therefore respectfully contend that they have established that TANGO 294 is a lipase.

The Applicants respectfully assert that because they have established that TANGO 294 protein is a lipase, that is sufficient to demonstrate that the claimed nucleic acid molecules have a specific, substantial, and credible utility. Reconsideration and withdrawal of the Examiner's rejection of all of the pending claims pursuant to 35 U.S.C. §101 are respectfully requested.

#### **Objections and Rejections Pursuant to 35 U.S.C. §112, First Paragraph**

The Examiner rejects all of the pending claims pursuant to the first paragraph of 35 U.S.C. §112.

In one aspect, the Examiner's rejection is based on the utility rejection made pursuant to 35 U.S.C. §101. The Applicants believe that the arguments made above with respect to the §101 rejection apply equally here, and that the Examiner should reconsider and withdraw the §112, first paragraph, rejection insofar as it is based on a purported lack of utility.

In a second aspect, the Examiner indicates that the §112, first paragraph, rejection is also based on a perceived incongruity between the scope of what is enabled and the scope of what is claimed. In particular, the Examiner suggests that no specific activity has been disclosed for TANGO 294 protein, and that the specification does not teach what portion of TANGO 294 comprises a biologically active or conserved region. The Examiner also objects to the scope imparted by the term "stringent conditions."

Use of the term "stringent conditions" has been discontinued in the claim, and specific hybridization conditions have been recited in their place. Because the recited hybridization conditions are useful for assessing hybridization of a recited nucleic acid with only very highly complementary nucleic acids, the Applicants respectfully contend that the scope of enablement of claims that recite the hybridization conditions is commensurate in scope with what is taught in the specification.

The Applicants disagree with the Examiner's contention that the specification does not disclose a specific activity for TANGO 294 protein. The specification discloses, at page 64, lines 29 and 30, that TANGO 294 is a lipase. Lipases exhibit lipase activity (i.e., the

ability to catalyze deacylation of acylglycerols). The Applicants respectfully contend that even if they are not able to differentiate the sequence of every fragment of TANGO 294 that exhibits lipase activity from the sequence of every fragment of TANGO 294 that does not exhibit lipase activity, they are not required to do so. Generating fragments of proteins (and nucleic acid molecules that encode such fragments) is routine in the art, as is screening protein fragments for lipase activity. Furthermore, the specification discloses (e.g., at page 77, line 10, through page 78, line 6, discloses how variant nucleic acid molecules encoding functional TANGO 294 proteins and fragments thereof can be made. The Applicants therefore respectfully contend that the specification enables a skilled artisan to make and use nucleic acid molecules encoding a biologically active fragment of TANGO 294 (i.e., a fragment that exhibits lipase activity).

With regard to the Examiner's comment regarding whether probes and primers would be sufficiently specific that they would bind only with a 'TANGO 294 polynucleotide' (the Examiner's term), the Applicants respectfully reply that this issue is irrelevant. The purpose of probes and primers is simply to bind with their complementary polynucleotides - not necessarily to bind exclusively with those polynucleotides. In certain circumstances (e.g., chromosome mapping), it is preferable that probes be exclusively specific for the TANGO 294 gene. However, the Applicants need only enable one use of the claimed nucleic acid molecules - not all conceivable uses. The Applicants respectfully contend that the specification discloses sufficient information to enable a skilled artisan to use all of the claimed nucleic acid molecules for at least one purpose disclosed in the specification.

For the foregoing reasons, the Applicants request that the Examiner reconsider and withdraw the rejection of all pending claims pursuant to 35 U.S.C. §112, first paragraph.

#### **Objections and Rejections Pursuant to 35 U.S.C. §112, Second Paragraph**

The Examiner rejects all of the pending claims pursuant to the second paragraph of 35 U.S.C. §112. The Examiner objects to the term "stringent conditions" in claims 1 (part e), 7 (part e), 32, and 37. The Applicants believe that the Examiner intended to object to claim 12 (part c) rather than to claim 7 (part e), since the term does not occur in claim 7, but does occur in claim 12. The other pending claims are objected to as depending from one of these claims.

Each of claims 1, 12, 32, and 37 has been amended to specify the stringent conditions referred to in the claim. The Applicants believe that these amendments render moot the Examiner's concern regarding the term "stringent conditions."

Reconsideration and withdrawal of the Examiner's rejection of all of the pending claims pursuant to the second paragraph of 35 U.S.C. §112 are respectfully requested.

**Summary**

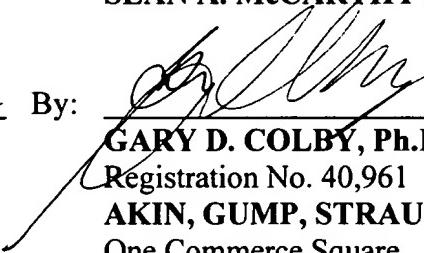
For the foregoing reasons, the Applicants respectfully contend that each of claims 1-7, 12, and 24-40 is in condition for allowance. Reconsideration of the Examiner's rejections and objections and allowance of the pending claims are respectfully requested at the earliest possible time.

Respectfully submitted,

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14 January 2002  
(Date)

By:

  
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Enclosures: Petition for Extension of Time  
Marked-Up Copy of Amended Claims  
Clean Copy of Claims, as Amended  
Executed Declaration and Power of Attorney  
Phylogenetic Tree